## REMARKS/ARGUMENTS

Upon entry of the amendment, claims 7, 9, 13, 15, 19, and 32-33, 35-36, and 38-44 will be pending in this application and presented for examination. Claims 7, 9, 13, 15, and 38-44 have been amended. Claims 31, 34 and 37 have been canceled without prejudice. The features of the canceled claims have been incorporated into the independent claims from which they depend. No new matter has been added with the foregoing amendments. Reconsideration is respectfully requested.

In this response, the Examiner's objections and rejections are addressed in the order set forth in the Office Action.

## I. CLAIM OBJECTIONS

The Examiner objected to claims 7, 9, 15 and 44 for various informalities. Applicants have taken the Examiner's helpful suggestions and incorporated the changes into the claims. In view of the changes and amendments to the claims, Applicants respectfully request that the Examiner withdraw the claim objections.

## II. FIRST REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 7, 9, 13, 15 and 19 under 35 U.S.C. § 103(a) as allegedly being obvious in view of the combination of WO 00/20028 ("Staats *et al.*") and *Kurume Med J., 2001,*Vol. 48, p. 171-174 ("Takasu"). To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

The Examiner states the following:

> Staats teaches a method of eliciting an immune response by administration of a vaccine antigen and an adjuvant (see abstract, and claim 1). Staats teaches that the vaccine antigen can be either protein or peptide antigens, including protein/peptide antigens from a number of pathogenic organisms (see p. 21, line 11 - p. 23, line 2). Staats also teaches that various cytokines can be used as adjuvants (see p. 14, line 19 - p. 15, line 2, and claims 5-6). Furthermore, Staats teaches mucosal administration of the vaccine adjuvant combination

> (claim 17), and also teaches that the vaccine-adjuvant induces both systemic (claim 22) and mucosal (claim 25) immune responses. Finally, by teaching that the vaccine and adjuvant are included together as a composition, Staats teach that the vaccine antigen and the adjuvant are administered at the same time and by the same route of administration. However, Staats is silent regarding the use of IFN-a as the adjuvant for any antigen-adjuvant combination or composition.

As the Examiner has pointed out, Staats *et al.* fail to teach an essential element of the claims *i.e.*, the specific adjuvant as is currently claimed. In an attempt to rectify this deficiency, the Examiner combines the teaching of Staats *et al.* with Takasu. The Examiner states:

> Takasu teaches that IFN-a is a potent adjuvant for increasing the immune response to various vaccine antigens. Specifically, Takasu discloses that co-administration of IFN-a with influenza virus peptide increased the cytotoxic T lymphocyte (CTL) response to the influenza virus peptide compared to vaccination with the influenza virus peptide alone (see p. 172-174, Figures 1-3).

However, Takasu simply does not teach nasal administration nor that the antibodies are secreted at the gastrointestinal mucosa as is currently claimed. Moreover, there is simply no indication that the method of Takasu invokes the humoral immune response by secreting antibodies as claimed and involving Th2 activation and cytokine production. The CTL induction as taught by Takasu is restricted to cell-mediated immunity which involves T-lymphocytes.

Takasu teaches that the antigen peptide is administered continuously by *osmotic pump*, while the INF-α is *injected* at the site of peptide inoculation. There is absolutely no teaching or suggestion of a nasal administration as is currently claimed, nor is there any teaching of the adjuvant and the peptide being administered as a composition at the same time.

Because the route of administration as described in Staats *et al.* is so much different than the use and methods of Takasu, there is no rational underpinning to support a legal

conclusion of obviousness. (*KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (U.S. 2007).

Accordingly, Applicants request that the Examiner withdraw the rejection.

## III. SECOND REJECTION UNDER 35 U.S.C. § 103(a)

Claims 7, 9, 13, 15, and 19 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,436,391 ("Foster *et al.*") in view of U.S. Patent No. 6,361,769 ("Tovey"). To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

The Examiner states:

> Foster teaches the use of IFN-a as a vaccine adjuvant to increase B lymphocyte proliferation, and thus increase the effectiveness of vaccines (column 1, lines 52-56), and specifically recites co-administration of a vaccine with IFN-a, or alternatively, a composition comprised of IFN-a and a vaccine (column 1, lines 61-65). Foster is silent regarding mucosal administration of an IFN-a vaccine-adjuvant composition, and is also silent regarding specific amounts or doses of IFN-a.
>
> Tovey teaches a method of stimulating host immunity by oromucosal administration of IFN-a (column 2, line 32 - column 3, line 28). Tovey discloses specific doses of IFN-a that can be oromucosally administered (column 3, line 15-20), and also teaches that IFN-a can be administered as adjunct to other therapy (column 3, lines 21-22), and specifically mentions previous studies in which IFNs where orally administered to enhance the efficiency of vaccines (column 1, lines 61-66).
>
> Foster *et al.* teaches the following:
>
> We have now found that B cell proliferation can be induced by certain IFN-$\alpha$ subtypes. Thus, it is possible to stimulate a subject's immune response and in particular the subtypes can be used as adjuvants to increase the effectiveness of vaccines.

> Thus, in a first aspect the present invention provides an adjuvant for a vaccine comprising an IFN-α subtype. In particular the invention provides an adjuvant for a vaccine which comprises IFN-α8 and/or IFN-α14.
>
> The adjuvant of the present invention can be co-administered with a vaccine or could itself form part of the vaccine itself. Thus, in a second aspect the present invention provides a vaccine comprising at least one IFN-α subtype, preferably IFN-α8 and/or IFN-α14. (see, column 1, lines 52-56).

However, Foster *et al.* clearly state that not all subtypes work. Foster *et al.* states as follows:

> The results show that all the IFN-α subtypes caused an increase in B cell proliferation, with the exception of IFN-α-1, which is inactive at the concentrations used in the experiment. (column 2, lines 31-34).

Given that some subtypes were effective and another subtype was totally ineffective, a skilled person would have no expectation of success of using IFN-α without separating the molecule into various subtypes.

Tovey teaches a method for stimulating the immune response by administering an interferon via oromucosal contact. There is no teaching or suggestion of a mucosal adjuvant comprising a natural interferon α *and* an antigen comprising a protein or peptide antigen being administered via the nasal mucosal eliciting a systemic immune response as well as a mucosal immune response. In other words, Tovey does not teach the antigen being present in the composition. Accordingly, Applicants request that the Examiner withdraw the rejection.

## IV. REJECTION UNDER 35 U.S.C. § 101

Claims 9 and 15 were rejected under 35 U.S.C. § 101 as allegedly reciting a "use," but being dependent on a composition. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Claims 9 and 15 were amended to delete the term "used." In view of this amendment, Applicants respectfully request that the Examiner withdraw the rejection.

## V. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

### 1. Claims 9 and 15

Claims 9 and 15 were rejected as allegedly being indefinite. To the extent this rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Claims 9 and 15 have been amended to more clearly define the invention. Accordingly, Applicants request that the Examiner withdraw the rejection.

### 2. Claim 40

Claim 40 was rejected as allegedly being indefinite. To the extent this rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Applicants have amended claim 40, and claim 19 to more clearly set forth the claimed invention. Accordingly, Applicants request that the Examiner withdraw the rejection.

### 3. Claims 40 and 41

Claims 40 and 41 were rejected as allegedly lacking sufficient antecedent basis for the limitation of "the entire composition." To the extent this rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Applicants have amended claims 40 and 41 to more clearly set forth the claimed invention. Accordingly, Applicants request that the Examiner withdraw the rejection.

### 4. Claim 43

Claim 43 was rejected as allegedly being indefinite for failing to define the acronym "PLGA." To the extent this rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Applicants have amended claim 43 to more clearly set forth the claimed invention by defining the acronym PLGA as --lactide-glycolide copolymer-- This is a term well known to those of skill in the art. Accordingly, Applicants request that the Examiner withdraw the rejection.

## VI. FIRST REJECTION UNDER 35 U.S.C. § 102(b)

Claims 7, 9, 13, 15, 19, and 31-39 were rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Takasu. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Under MPEP § 2131:

> [a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claims 7, 13, and 19 have been amended to recite that the vaccine antigen-specific antibody is secreted at the gastrointestinal mucosal surface. The feature is a humoral immune response, which involves Th2 activation and cytokine production. This feature is not described. The CTL induction of Takasu is restricted to cell-mediated immunity which involves T lymphocytes. As each and every element of the claim must be in the cited reference, Applicants respectfully request that the Examiner withdraw the rejection.

## VII. SECOND REJECTION UNDER 35 U.S.C. § 102(b)

Claims 7, 9, 13, 15, 19 and 31-39 are rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Tovey. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Under MPEP § 2131:

> [a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a

> single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Tovey teaches a method for stimulating the immune response by administering an interferon via oromucosal contact. There is no teaching or suggestion of a mucosal adjuvant comprising a natural interferon α *and* an antigen comprising a protein or peptide antigen being administered via the nasal mucosal eliciting a systemic immune response as well as a mucosal immune response. In other words, Tovey does not teach the antigen being present in the composition. As each and every element of the claim must be in the cited reference, Applicants respectfully request that the Examiner withdraw the rejection.

## VIII. THIRD REJECTION UNDER 35 U.S.C. § 102(b)

Claims 7, 9, 13, 15, 19 and 31-39 are rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Foster *et al.* To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Under MPEP § 2131:

> [a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Foster *et al.* teach "[w]e have now found that B cell proliferation can be induced by certain IFN-α subtypes." Column 1, lines 52-53). Clearly, the specification and claims of Foster *et al.* only teach the use of a IFN-α subtype not IFN-α as claimed. As each and every element of the claim must be in the cited reference, Applicants respectfully request that the Examiner withdraw the rejection.

## IX. THIRD REJECTION UNDER 35 U.S.C. § 103(a)

Claim 41 was rejected as allegedly obvious under 35 U.S.C. § 103(a) over either Takasu or Tovey or Foster *et al.* To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Claim 41 depends upon claim 19. Claim 19 is unobvious as set forth above. As claim 19 is not obvious then claim 41 cannot be obvious because it depends from a nonobvious claim. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) ("[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious."). Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

## X. FOURTH REJECTION UNDER 35 U.S.C. § 103(a)

Claims 42-44 are rejected as allegedly being obvious under 35 U.S.C. § 103(a) over Takasu in view of Kawashima *et al.* In response, Applicants respectfully traverse the rejection.

Takasu has been discussed. Kawashima *et al.* has nothing at all to do with nasal administration of a vaccine as claimed. In the abstract, Kawashima *et al.* teach oral administration. There is absolutely no teaching or suggestion of using the composition as claimed. Further, "dependent claims are nonobvious if the independent claims from which they depend are nonobvious." (*In re Fritch,* 972 F.2d 1260, 1266 (Fed. Cir. 1992)). Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

## XI. FIFTH REJECTION UNDER 35 U.S.C. § 103(a)

Claims 42-44 are further rejected as allegedly being obvious over Tovey in view of Kawashima *et al.* The Examiner states that Tovey is silent with regard to encapsulation, but Kawashima *et al.* supplies this teaching. In response, Applicants respectfully traverse the rejection.

Tovey has been discussed. Kawashima *et al.* has nothing at all to do with nasal administration of a vaccine composition as claimed. In the abstract, Kawashima *et al.* teach oral

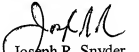
administration. There is absolutely no teaching or suggestion of using the composition as claimed. Further, "dependent claims are nonobvious if the independent claims from which they depend are nonobvious." (*In re Fritch,* 972 F.2d 1260, 1266 (Fed. Cir. 1992)). Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

## XII. CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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